P045529PCT

New CLAIMS (20 December 2004)

1. Use of an instrument for measuring a Raman signal of tissue, the instrument comprising a laser, a signal detection unit for measuring the Raman signal, and a fiber optic probe, wherein the fiber optic probe comprises one or more optical fibers for directing laser light onto the tissue and for collecting light that is scattered by the tissue and guiding the collected light away from the tissue towards the signal detection unit, the fiber comprising a core, a cladding and optionally a coating, and the fiber or fibers for collecting light having substantially no Raman signal in one or more parts of the 2500-3700 cm^{-1} spectral region, and wherein the detection unit records the Raman signal scattered by the tissue in said spectral region, wherein the fiber has substantially no Raman signal in one or more parts of the 2500-3700 cm^{-1} spectral region, the instrument further comprising a signal analysis unit which analyses the recorded Raman signal in one or more parts of the 2500-3700 cm^{-1} spectral region, the analysis comprising an algorithm which outputs data regarding the molecular composition of the tissue and/or the clinical diagnostic class to which the tissue belongs.

2. Use of an instrument according to claim 1, wherein the fiber optic probe comprises an optical fiber that both directs laser light onto the tissue and collects light that is scattered by the tissue and guides the collected light away from the tissue towards the signal detection unit.

3. Use of an instrument according to one of the preceding claims, wherein the fiber optic probe comprises at least one fiber having a low OH^- fused silica core.

4. Use of an instrument according to one of the preceding claims, wherein the fiber optic probe comprises at least one optical fiber having a fused silica core and a fused silica or Teflon or TECS cladding.

5. Use of an instrument according to one of the preceding claims, wherein the coating of the optical fiber comprises one or more of Teflon coatings and metal coatings.

6. Use of an instrument according to one of the preceding claims, wherein the detection unit substantially measures only the signal obtainable from the core of the optic fiber.

7. Use of an instrument according to one of the preceding claims, wherein Raman measurements can be combined with fluorescence and/or near-infrared absorption measurements and wherein the detection unit also comprises a detection unit for measuring the intensity and/or spectrum of tissue fluorescence and/or a detection unit for measuring near-infrared absorption.

8. Use of an instrument according to claim 7, wherein fluorescence and/or near-infrared absorption measurements make use of a fiber also used in obtaining Raman signal.

9. Use of an instrument according to one of the preceding claims, wherein the fiber optic probe is brought in, or in contact with, or in proximity to the tissue under investigation.

P045529PCT

10. Use of an instrument according to one of the preceding claims, wherein the tissue is excised, biopted or taken from a human or animal body before measuring.

11. An instrument for measuring a Raman signal of tissue, the instrument comprising a laser, a signal detection unit for measuring the Raman signal, and a fiber optic probe, wherein the fiber optic probe comprises one or more optical fibers for directing laser light onto the tissue and for collecting light that is scattered by the tissue and guiding the collected light away from the tissue towards the signal detection unit, the fiber comprising a core, a cladding and optionally a coating, and the fiber or fibers for collecting light having substantially no Raman signal in one or more parts of the 2500-3700 cm^{-1} spectral region, and wherein the detection unit records the Raman signal scattered by the tissue in said spectral region, and wherein the fiber has substantially no Raman signal in one or more parts of the 2500-3700 cm^{-1} spectral region, the instrument further comprising a signal analysis unit which analyses the recorded Raman signal in one or more parts of the 2500-3700 cm^{-1} spectral region, the analysis comprising an algorithm which outputs data regarding the molecular composition of the tissue and/or the clinical diagnostic class to which the tissue belongs.

12. Instrument according to claim 11, wherein the fiber optic probe comprises an optical fiber that both directs laser light onto the tissue and collects light that is scattered by the tissue and guides the collected light away from the tissue towards the signal detection unit.

13. Instrument according to claim 11 or 12, wherein the fiber optic probe comprises at least one fiber.

14. Instrument according to one of claims 11-13, wherein the fiber optic probe comprises at least one optical fiber having a fused silica core and a fused silica or Teflon or TECS cladding.

15. Instrument according to one of claims 11-14, by using a coating material in which intrinsically little or substantially no signal is generated in the 2500-3700 cm^{-1} wavenumber interval.

16. Instrument according to one of claims 11-15, wherein the coating of the optical fiber comprises one or more of Teflon coatings and metal coatings.

17. Instrument according to one of claims 11-16, wherein the fiber comprises a first and a second coating, the first coating as coating on the cladding and the second coating as coating on the first coating, wherein the second coating comprises a laser light absorbing material.

18. Instrument according to one of claims 11-17, wherein the fiber comprises a first and a second coating, the first coating as coating on the cladding and the second coating as coating on the first coating, wherein the second coating comprises a material having a higher refractive index than the first coating material.

ART 34 AMDT

19. Instrument according to one of claims 11-18, wherein the detection unit also comprises a detector for measuring fluorescence and/or a detector for near-infrared absorption.

20. Instrument according to one of claim 19 wherein fluorescence and/or near-infrared absorption measurements make use of a fiber also used in obtaining Raman signal and wherein the detection unit also comprises a detector for measuring fluorescence and/or a detector for near-infrared absorption.

21. Instrument according to one of claims 11-20 wherein the fiber optic probe comprises a bundle of fibers for measuring and/or scanning a tissue area.

22. Instrument according to one of claims 11-21, wherein the fiber optic probe comprises one optical fiber, the fiber having substantially no Raman signal in one or more parts of the 2500-3700 cm^{-1} spectral region.

23. Instrument according to one of claims 11-22, wherein the optical fiber comprises a laser light absorbing end tip coating.

24. Instrument according to one of claims 11-23, wherein the end face of the optical fiber, where the laser light is coupled into the optical fiber, is polished.

25. A method for producing and measuring a Raman signal of tissue, comprising providing a laser, a detection unit for measuring a Raman signal, and a fiber optic probe, wherein the fiber optic probe comprises one or more optical fibers for directing laser light onto the tissue and for collecting light that is scattered by the tissue and guiding the collected light away from the tissue toward the signal detection unit, the fiber comprising a core, a cladding and optionally a coating; sending laser light through the one or more optical fibers, receiving the Raman signal from the tissue through the one or more optical fibers and detecting the Raman signal by a signal detection unit, the fiber or fibers for collecting light having substantially no Raman signal in one or more parts of the 2500-3700 cm^{-1} spectral region, and wherein the signal detection unit records the Raman signal in said spectral region, and wherein the fiber has substantially no Raman signal in one or more parts of the 2500-3700 cm^{-1} spectral region, the instrument further comprising a signal analysis unit which analyses the recorded Raman signal in one or more parts of the 2500-3700 cm^{-1} spectral region, the analysis comprising an algorithm which outputs data regarding the molecular composition of the tissue and/or the clinical diagnostic class to which the tissue belongs

26. Method according to claim 25, further comprising sending the laser light through a same optical fiber which also receives the Raman signal, using an optical fiber for this method which has substantially no Raman signal in one or more parts of the 2500-3700 cm^{-1} spectral region

27. A method for measuring a Raman signal of a tissue sample, wherein an instrument according to one of claims 11-24 is used and wherein the tissue sample is excised, biopied or taken from a human or animal body before measuring.

P045529PCT

28. Method for evaluating an optical fiber for measuring a Raman signal of tissue, wherein an instrument according to one of claims 11-24 is used and wherein a tissue sample is excised, biopted or taken from a human or animal body before measuring, and wherein the Raman signal of the optical fiber is measured of the sample and of a blanc, and wherein the Raman signals of the sample and of the blanc are compared.

29. Method for evaluating the suitability of a type of fiber for measuring the Raman signal of tissue, comprising:
- using an instrument according to one of claims 11-24
- performing a measurement without tissue being present at the distal end of the fiber,
- performing a measurement with tissue being present at the distal end of the fiber,
- comparing the spectra obtained with and without tissue being present
- concluding that the fiber is suitable for measuring the Raman signal of tissue.

30. Instrument according to one claims 11-24, wherein part of the fiber is integrated or combined with a catheter that provides additional information about the tissue or which comprises means to obtain tissue samples, means to treat tissue and/or means used in surgical procedures.

31. Instrument according to one of claims 11-24, wherein the fiber optic probe comprises one single optical fiber.

32. Instrument according to one claims 11-24, wherein a mask over the fiber end face is applied, which only leaves the fiber core uncovered.

33. Instrument according to one of claims 11-24, wherein the coating of the optical fiber comprises an acrylate coating.

34. Use according to one of claims 1-10, for measuring a Raman signal of a tissue sample prior to it being resected, or biopted or for selecting tissue for biopsy or resection.

35. A method for measuring a Raman signal of a tissue sample, wherein an instrument according to one of claims 11-24 is used and wherein a Raman signal of a tissue sample is measured prior to it being resected or biopted.

36. A method for measuring a Raman signal of a tissue sample, wherein an instrument according to one of claims 11-24 is used and wherein a Raman signal of a tissue sample is measured for selecting this tissue for biopsy or resection.

ART 34 AMDT